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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 05/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/202,464	KINO ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,29-35 and 38-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1,5,29-35,38 and 39* is/are allowed.

6)☒ Claim(s) *40-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/5/04 has been entered.

2. Claims 1, 5, 29-35 and 38-46 are pending and are being acted upon in this Office Action.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 41-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for peptides as set forth in claims 1, 29-31, 38 and 39, composition comprising said peptides (claims 5, and 32-35) and methods of treating and diagnosing pollinosis, **does not** reasonably provide enablement for (1) a method for "preventing" pollinosis caused by tree pollen in springtime comprising administering the peptide of claim 1 or claim 39 to an individual susceptible to pollinosis, (2) a method of diagnosis pollinosis by determining any responsiveness of the lymphocytes to the peptide of claim 39 as set forth in claims 43-44 and (3) *any* analog peptide or modified peptide as set forth in claim 45-56. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only the specific peptides as set forth in claim 1 and 39 for a method of treating pollinosis and diagnosis of pollinosis by determining T cell proliferation in response to said peptides.

The specification does not teach how to "prevent" pollinosis by administering any peptide such as the ones recited in claims 1 and 39 or any analog peptide because there is insufficient in vivo working example demonstrating that the claimed method can prevent pollinosis. The term "preventing" is problematic because the term "prevent" as define by the Webster's II New Riverside University Dictionary as "to keep from happening or to anticipate or counter in advance". The specification fails to provide guidance as how to select or identify an individual before allergy symptoms begin, how to predict who would or would not get allergy, let alone "preventing" allergy from happening.

With regard to claims 43 and 44, the specification does not teach how to diagnosis pollinosis by contacting lymphocytes with a peptide of claim 1 or 39 and determining any "responsiveness" of all lymphocytes as an indication of the individual is susceptible to pollinosis. The term "responsiveness" encompasses inhibitory and stimulatory response which are mutually exclusive. It fails to indicate which particular response. The specification discloses only T lymphocytes proliferation as a response to the peptide set forth in claims 1 and 39. Other than T cell proliferation in the presence of the peptide as an indication of pollinosis, the other response is not adequately taught in the specification as filed.

With regard to "analog peptide" and "modified peptide", the specification does not teach how to make all "analog peptide" and "modified peptide" because there is insufficient guidance as to the structure of the "analog peptide" and "modified peptide" without the specific amino acid sequence (SEQ ID NO). Further, there is insufficient guidance as to which amino acids within the peptide to be substitute for which undisclosed amino acids, and whether the resulting peptide maintains binding to the T cell receptor or MHC class II, and stimulates T cell proliferation or stimulate T cells to produce a greater amount of interferon gamma than the wild type peptide.

Stryer *et al* teach that a protein is highly dependent on the overall structure of the protein itself and that the primary amino acid sequence determines the conformational of the protein (See enclosed appropriate pages).

Ngo *et al* teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are

critical to maintain the protein's structure/function will require guidance (See Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

It has been well known to those skilled in the art at the time the invention was made that minor structural differences among structurally related compounds or compositions could result in substantially different pharmacological activities. Fasler *et al* teach that peptides derived from house dust mite Der p1 are modified by even a single amino acid substitutions at positions 173, 175, 176, 180 and 181 with alanine or glycine failed to induce Der p1 specific T cell proliferation and IL-2, IL-4 and IFN-γ production. Fasler *et al* further teach that substituting a neutral amino acid residue such as Asn at position 173 with either a basic Lysine, which is a hydrophobic amino acid residue did not induce T cell proliferation and cytokine production. However, substitution amino acid positions other than 173, 175, 176, 180 and 181 induces normal or only slightly reduced proliferative responses and cytokine production by T cells (page 524, in particular). Further, there are insufficient in vivo working examples demonstrating that the undisclosed analog peptide and modified peptide is effective for treating pollinosis, let alone for preventing pollinosis.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

5. Claims 43-46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of a method of diagnosis pollinosis by determining any responsiveness of the lymphocytes to the peptide of

claim 39 as set forth in claims 43-44 and (3) *any* analog peptide or modified peptide as set forth in claim 45-56.

The specification discloses only the specific peptides as set forth in claim 1 and 39 for a method of treating pollinosis and diagnosis of pollinosis by determining T cell proliferation in response to said peptides.

With the exception of the specific peptides as set forth in claims 1, 29-31, 38 and 39 for a method of treating pollinosis or diagnosis, there is insufficient written description about the structure associated with function of *any* analog peptide or modified peptide without the amino acid sequence.

With regard to claims 43 and 44, there is insufficient written description about any "responsiveness" of all lymphocytes is an indication of an individual susceptible to pollinosis. The term "responsiveness" encompasses inhibitory and stimulatory response which are mutually exclusive. The specification discloses only T lymphocytes proliferation in response to the peptides set forth in claims 1 and 39 as an indication of individual is susceptible to pollinosis. Other than T cell proliferation, the other responses of all lymphocyte such as inhibitory response as a method of diagnosis is not adequately described. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398; University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC2004).*

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

6. Claim 40 is rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

The term "consisting essentially of" in claim 40 has no support in the specification and the claims as originally filed. Applicant has not point out the support for said "consisting essentially of" comes from. Note, if the composition is intended to be close, it is suggested that

the claims be recite "consisting of"; if the composition is intended to be open, it is suggested that the claims be recite "comprising".

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claims 43-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The preamble "A method of diagnosis" of claims 43 and 44 is ambiguous and indefinite because it is not clear the claimed method is diagnosis of what particular disease. Further, the term "responsiveness of lymphocytes" in claims 43 and 44 is not clear as to which particular response such as inhibition of T cell response or stimulation of T cell proliferation or interferon gamma secretion is part of the claimed method. One of ordinary skill in the art cannot appraise the metes and bound of the claimed invention.

The "...analog peptide stimulates a T cell that is responsive to the wild-type peptide" in claim 45, line 4 is ambiguous and indefinite because it is not clear what is meant by responsive to the wild-type peptide. One of ordinary skill in the art cannot appraise the metes and bound of the claimed invention.

The "modified peptide" in claim 46 has no antecedent basis in base claim 46 because claim 45 recites an analog peptide instead of modified peptide.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 45-46 are rejected under 35 U.S.C. 102(b) as being anticipated by WO94/01560 publication (of record, Jan 1994; PTO 1449).

The WO 94/01560 publication teaches an analog peptide consisting of GATR**D**R**P**LWIIFS**G**N**M**NIKL which is analog peptide of the claimed sequence GATRERSLWIIFSKNLNIKL of SEQ ID NO: 9 (see reference peptide CJI-7, Fig 13, in

particular). The reference peptide has more than one amino acid substitutions and stimulates a T cell proliferation (See bold letter above and claims 119-120 of WO 94/01560 publication, in particular). Since the reference analog peptide appears to be the same as the claimed analog peptide, the reference analog peptide inherently produces interferon gamma equal to or greater than the wild-type peptide, especially the reference peptide is use for reducing the symptoms of Japanese cypress pollinosis or cedar pollinosis (See claims 64 and 68 of WO 94/01560, in particular). Since the Patent Office does not have the facilities for examining and comparing the antibodies of the instant invention to those of the prior art, the burden is on applicant to show that the prior art antibody is different from the claimed antibody. See *In re Best*, 562 F.2d 1252, 195 USPQ 430(CCPA 1977). Thus, the reference teachings anticipate the claimed invention.

11. Claims 1, 5, 29-35, 38 and 39 are allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (703) 872-9306.

13. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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